International Cancer Conference Journal (2021) 10:244–247
https://doi.org/10.1007/s13691-021-00489-9

CASE REPORT

Histiocytic sarcoma arising from a lymph node: a diagnostic conundrum

Anoshia Afzal[1] · Sepideh N. Asadbeigi[2] · Umar Farooque[3] · Christy Mather[4] · Shahbaz Khan[5]

Received: 15 December 2020 / Accepted: 5 May 2021 / Published online: 21 May 2021

Abstract

Histiocytic Sarcoma (HS) is extremely rare, with only a few hundred cases reported in the literature. The majority of patients present with symptoms due to unifocal or multifocal extra-nodal disease. Less than 20% of these cases show solitary involvement of a lymph node. We report a case of a solitary HS in a 53-year-old woman presenting with a 2.7-cm right groin mass arising from an inguinal lymph node. The initial cytologic examination of the tissue showed a high-grade spindle-shaped morphology with high-grade mitotic activity. A high-grade sarcoma was initially considered considering the absence of normal lymphoid aggregate and the presence of high-grade cytologic features in the cells. To evaluate the tumor in its entirety, the mass was surgically excised. A histological examination of the tumor showed focal rimming of the lymphoid tissue at the periphery and a centrally located stellate necrotic focus. The tumor cells had an epithelioid to spindle cell morphology along with large uniform nuclei and prominent nucleoli. A high mitotic index was present. Immunohistochemistry (IHC) stains showed strong positivity for CD68, CD163, and Vimentin, and were weakly positive for SMA and CD45. Based on the histologic and clinical examination, a diagnosis of HS was made. Multiple malignancies can mimic HS histopathology and the rarity of this tumor makes the diagnosis more challenging. No fine-needle aspiration (FNA) criteria for its diagnosis have been recognized. Herein, we report a rare case of an isolated HS involving a lymph node which resembled high-grade sarcoma on the FNA biopsy to raise awareness among our surgical pathologist colleagues.

Keywords Histiocytic sarcoma · Lymph node · Sarcoma

Introduction

Histiocytic Sarcoma (HS) is an extremely rare non-Langerhans histiocyte disorder. This disorder is characterized by the multiplication of malignant cells having characteristics of mature histiocytes [1]. The etiology of HS is unknown. HS is mainly seen in adults (mean age being 46 years); however, pediatric histiocytic sarcoma cases have been reported. It has a slight male predominance [2].

The symptoms appear most commonly due to the involvement of unifocal or multifocal extra-nodal tumors including spleen, soft tissue, lung, nasal cavity, lungs, brain, gastrointestinal tract, and skin [2–4]. Patients may present with hepatosplenomegaly, adenopathy and non-specific systemic symptoms like fever, weight loss, anorexia, and asthenia, which are common presentations in patients with HS [5]. In a few cases, asymptomatic involvement of the organs is incidentally discovered on imaging [6].

The pretreatment work-up for HS should include initial histologic confirmation, complete blood count, liver and renal function tests, a computerized tomography (CT) scan, and *positron emission tomography* (*PET*) imaging modalities for evaluating organ involvement and bone marrow biopsy [7].

The pathogenesis of HS is ambiguous. Being derived from cells of monocytic and macrophage systems, HS

✉ Sepideh N. Asadbeigi
Sepideh.asadbeigi@northwestern.edu

1 Department of Pathology, The University of Oklahoma Health Science Center, Oklahoma City, OK, USA

2 Department of Dermatopathology, McGaw Medical Center of Northwestern University, Suite 1600, 676 North Saint Clair Street, Chicago, IL 60611, USA

3 Department of Neurology, Dow University of Health Sciences, Karachi, Pakistan

4 Department of Psychology, University of Tulsa, Tulsa, OK, USA

5 Department of Pathology, Indiana University School of Medicine, Indianapolis, IN, USA

cannot be regarded as a true sarcoma. It is commonly associated with follicular lymphoma, acute myeloid leukemia, and acute lymphoblastic leukemia [8].

HS often presents with a solid tumor composed of sheets of large epithelioid cells with abundant rare mitotically active and necrosis is present. The IHC is necessary for diagnosis and shows positivity in CD68 and CD163. The literature is suggestive of positivity for at least two of CD68, CD163, CD4, and lysozymes for diagnosis [9, 10].

The diagnosis of HS is based on the anatomo-pathological evaluation of the involved tissue along with clinical correlation. It is important to note immunohistochemistry (IHC) is used to establish the diagnosis. It is important to note that less than 20% of HS cases show solitary involvement of a lymph node. Diagnosis is challenging, because these tumors are rare and consideration must be given to other differential diagnoses, including histiocytic and dendritic cell disorders, metastatic solid or hematopoietic neoplasms, primary familial lymphohistiocytic disorders, sarcomas, carcinomas, and acquired causes of hemophagocytic macrophage activation syndromes [10].

Given the rarity of this tumor and no known treatment protocol, accurate diagnosis is crucial for treatment planning. We are presenting a diagnostically challenging case to emphasize the clinicopathologic features of these rare tumors and to raise awareness among our pathologist colleagues.

Case presentation

We report a case of a solitary HS arising from an inguinal lymph node in a 53-year-old asymptomatic woman who presented with a groin mass and no known previous history of hematologic disease. Radiology revealed a 2.7-cm right inguinal mass without intra-pelvic, intra-abdominal, or thoracic lymphadenopathy. All the base line laboratory work-up, including complete blood count, comprehensive metabolic panel, and urine analysis were within normal limits. The fine-needle aspiration (FNA) biopsy revealed pleomorphic and high-grade cells with spindle cell morphology in the background of mixed inflammation. Those cells were weakly positive with smooth muscle actin (SMA) which raises the diagnosis of a high-grade sarcoma, such as leiomyosarcoma or a myofibroblastic tumor.

Considering the rarity of intra-nodal HS, HS was not the most suspected differential diagnosis and the surgical team resected the tumor. The subsequent resection demonstrated a nodule consistent with a lymph node involving extensive replacement by a neoplasm with focal riming of lymphoid tissue at the periphery and a small, centrally located stellate necrotic focus. The tumor invaded through the capsule into the surrounding adipose tissue.

The tumor shows an epithelioid to spindle cell morphology with large uniform nuclei and prominent nucleoli. Mitoses were easily seen with up to 28 mitotic figures per 10 high power field. IHC stains were strongly and diffusely positive for CD68, CD163, Vimentin, weakly positive SMA and CD45 and negative for Pan-Cytokeratin, Sox10, S100, MitF, CD15, CD30, Pax5, CD3, CD20, ALK protein, Cytokeratin 5/6, CD56, CD1a, CD21, CD23, and Clusterin (Fig. 1).

No follow up could be conducted, because the patient never returned to our facility after the re-excision surgery.

Discussion

Histiocytic sarcoma commonly presents as a solitary mass at an extra-nodal site [11]. This case presented with a mass originating from an inguinal lymph node without any extranodular involvement.

HS prognosis is poor and correlates with the staging of the disease and tumor size [1]. Interventions such as surgery, radiotherapy, chemotherapy, and their combinations are often required for the management of the disease and should be determined on a case-by-case basis [2, 12].

The role of the anatomo-pathological test of the afflicted organ or tissue in giving a definite diagnosis in case of histiocytic sarcoma is undisputed. Complete or incomplete effacement of the lymph nodes is common when they are affected by histiocytic proliferation of the malignant cells. There is much variability in the degree of cellular pleomorphism and mitotic activity. Abundant eosinophilic cytoplasm with vacuolated or foamy appearance is seen in most malignant cells. A noticeable single irregular nucleolus and oval nucleus containing vesicular chromatin that is eccentrically located is commonly seen in these malignant cells. Multiple nucleoli in multinucleated cells may also be found. Due to such variability, immunophenotyping and molecular studies are significant in diagnosing HS [10, 13].

In this case, the tumor shows an epithelioid and spindle cell morphology with a large uniform nucleus and a prominent nucleolus. Even though focal areas of spindled cells can be seen in HS, extensive spindling is rare. The lack of monster cells, abundant vacuolated cytoplasm, and a neutrophilic rich background, which are frequently seen in HS, diverts the attention from HS diagnosis on FNA. However, some other non-specific features of the tumor cells in our patient, such as a high mitotic index and necrosis, are frequently reported in HS [10]. One of the most challenging and unique features in this case is the positive SMA expression which is not one of the positive HS immunohistochemical markers and raises the unclassified pleomorphic sarcomas, leiomyosarcoma, and myofibroblastic tumors in the differential diagnosis. In cases like this, the diagnosis is made with confirmation of histiocytic lineage through immunophenotyping

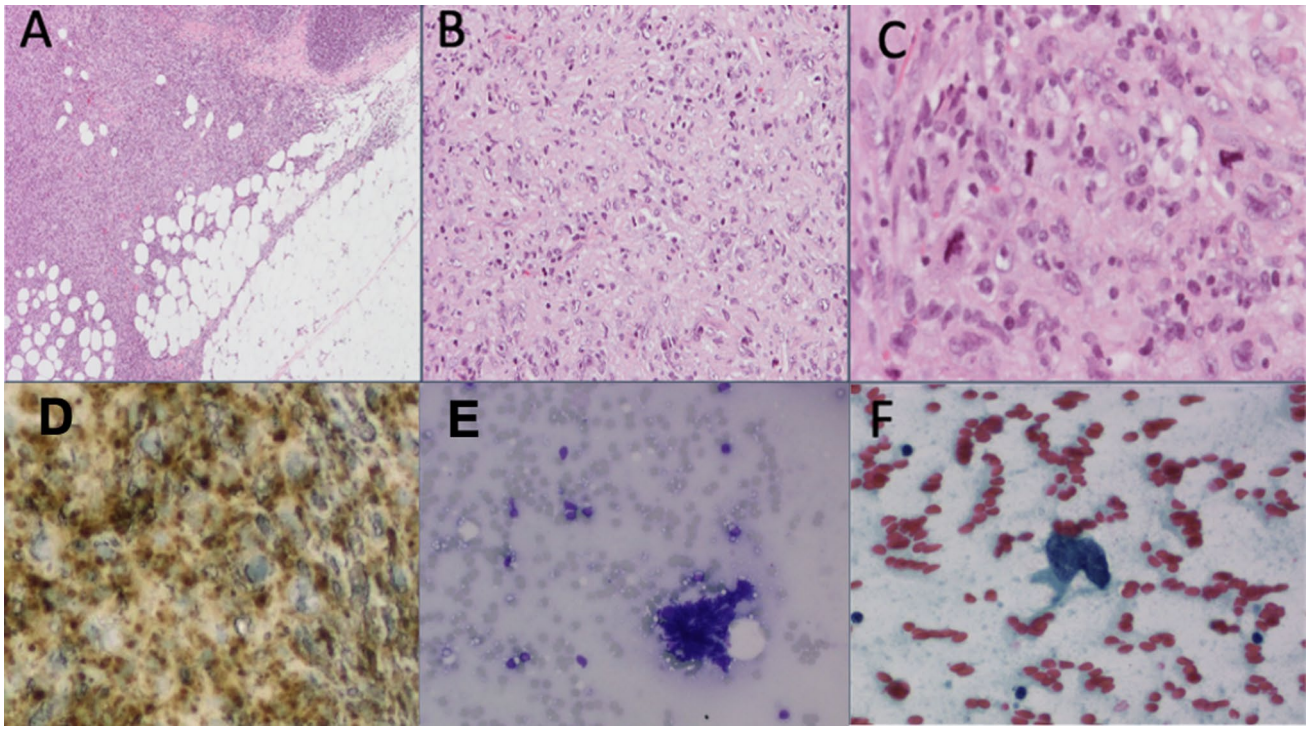

Fig. 1 **a** Hematoxylin and Eosin (H and E), 4×10, lymph node with a nodular infiltrate, and focal riming of lymphoid tissue at the periphery. **b** H and E, 20×10, tumor cells show an admixed of epithelioid to spindle cell morphology with large uniform nuclei and prominent nucleoli. **c** H and E, 40×10, frequent mitoses are easily seen with up to 28 mitotic figures per 10 high power field. **d** CD68 IHC, 40×10, diffuse and strong expression. **e** FNA, Diff-Quick stain, 20×10, highly pleomorphic cells in background of inflammatory cells. **f** FNA, Papanicolaou stain, 40×10, a large malignant cell with high-grade atypia and irregular border

by positive expression of CD68, lysozyme, and CD163. In addition, there is a negative expression of CD1a, CD21, and CD35 [14]. In this case, IHC stains were strongly and diffusely positive for CD68 and CD163, Vimentin; weakly positive for SMA and CD45; and negative for Pan-Cytokeratin, Sox10, S100, MitF, CD15, CD30, Pax5, CD3, CD20, ALK protein, cytokeratin 5/6, CD56, CD1a, CD21, CD23, and Clusterin.

The differential diagnosis of HS is broad and may be impacted by the location and morphology of the cells. Histiocytic diseases such as Langerhans cell histiocytosis may be misdiagnosed as HS. The HS cells can also mimic lymphomas, especially in cases of intra-nodal involvement or CD3/CD4 expression. However, the lack of most B- and T-cell markers can be used to exclude lymphomas. HS arising from soft tissue may be mistaken for sarcomas. The spindle shape morphology which is seen in some subsets and high-grade features can be seen in both HS and sarcomas. In the presented case, even though HS is not arising from the soft tissue, the spindle morphology and weak SMA positivity can be suggestive of sarcoma such as leiomyosarcoma. However, the SMA expression is not strong enough for an unequivocal diagnosis and the additional IHC on the resected specimen ruled out the sarcoma differential diagnosis. When HE is involving the skin, melanoma, juvenile xanthogranuloma, or desmoplastic squamous cell carcinoma can be considered in the differential diagnosis [11, 15]. Langerhans cell histiocytosis, Langerhans cell sarcoma, and melanoma have S100 expression. In a subset of HS, S100 can be expressed which complicates the diagnosis [16, 17]. Poorly differentiated carcinoma also can overlap with HS [2, 9]. All of the mentioned differential diagnoses are excluded based on the IHC and diagnosis HS by cytomorphology alone is extremely challenging. When epithelioid large cells with multinucleation and lymphoid background are not present, HS diagnosis would be heavily dependent on the IHC and exclusion of the other possible differential diagnoses [15]. Even though FNA is used for patients with extra-nodal HS, the limitation of diagnostic material and need for extensive IHC and molecular testing makes FNA more useful in assessing the disease recurrence rather than a primary diagnosis tool.

Conclusions

The diagnosis of HS in the lymph nodes, especially as a solitary node/mass, is challenging due to its rarity and the broad range of differential diagnoses. This case demonstrates a rare

presentation of HS in a 2.7-cm right inguinal mass arising from a lymph node which was almost entirely replaced the lymphoid tissue. In FNA and when the biopsy is limited, the representative cells may show an unusual histology. In such cases, IHC is the only diagnostic tool. However, to apply the correct IHC, such a rare entity such as HS should be considered in the differential diagnosis. The information presented will add to the growing body of HS literature to better inform early diagnosis and establish presentation characteristics associated with solitary involvement of a lymph node.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Alexiev BA, Sailey CJ, McClure SA, Ord RA, Zhao XF, Papadimitriou JC (2007) Primary histiocytic sarcoma arising in the head and neck with predominant spindle cell component. Diagn Pathol 2:7
2. Hornick JL, Jaffe ES, Fletcher CD (2004) Extranodal histiocytic sarcoma: clinicopathologic analysis of 14 cases of a rare epithelioid malignancy. Am J Surg Pathol 28(9):1133–1144
3. Oka K, Nakamine H, Maeda K et al (2008) Primary histiocytic sarcoma of the spleen associated with hemophagocytosis. Int J Hematol 87(4):405–409
4. Cheuk W, Walford N, Lou J et al (2001) Primary histiocytic lymphoma of the central nervous system: a neoplasm frequently overshadowed by a prominent inflammatory component. Am J Surg Pathol 25(11):1372–1379
5. Kobayashi S, Kimura F, Hama Y et al (2008) Histiocytic sarcoma of the spleen: case report of asymptomatic onset of thrombocytopenia and complex imaging features. Int J Hematol 87(1):83–87
6. Pileri SA, Grogan TM, Harris NL et al (2002) Tumours of histiocytes and accessory dendritic cells: an immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. Histopathology 41(1):1–29
7. Yaman E, Ozturk B, Erdem O et al (2008) Histiocytic sarcoma: PET-CT evaluation of a rare entity. Ann Nucl Med 22(8):715–717
8. deMent SH (1990) Association between mediastinal germ cell tumors and hematologic malignancies: an update. Hum Pathol 21(7):699–703
9. Emile JF, Abla O, Fraitag S et al (2016) Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 127(22):2672–2681
10. Hung YP, Qian X (2020) Histiocytic sarcoma. Arch Pathol Lab Med 144(5):650–654
11. Skala SL, Lucas DR, Dewar R (2018) Histiocytic sarcoma: review, discussion of transformation from B-cell lymphoma, and differential diagnosis. Arch Pathol Lab Med 142(11):1322–1329
12. De Vos FY, Gerding MN, Arends JW, Wegman JJ (2008) Histiocytic sarcoma localised in the thyroid: a case report. Ann Hematol 87(8):681–682
13. Khosravi Shahi P, del Castillo RA (2005) Histiocytic sarcoma: a case report and review of the literature. An Med Interna 22(4):185–187
14. Machado ES, de Miranda AC, Escopelli T, Caron R, Escopelli AC (2011) Histiocytic sarcoma. Rev Bras Hematol Hemoter 33(2):155–157
15. Hung YP, Lovitch SB, Qian X (2017) Histiocytic sarcoma: New insights into FNA cytomorphology and molecular characteristics. Cancer Cytopathol 125(8):604–614
16. Shao H, Xi L, Raffeld M et al (2011) Clonally related histiocytic/dendritic cell sarcoma and chronic lymphocytic leukemia/small lymphocytic lymphoma: a study of seven cases. Mod Pathol 24(11):1421–1432
17. Dalia S, Jaglal M, Chervenick P, Cualing H, Sokol L (2014) Clinicopathologic characteristics and outcomes of histiocytic and dendritic cell neoplasms: the moffitt cancer center experience over the last twenty five years. Cancers (Basel) 6(4):2275–2295